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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
SULLIVAN, DANIEL M	

ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 05/12/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/997,425	EDINGER ET AL.	
	Examiner	Art Unit	
	Daniel M. Sullivan	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 February 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *5,8,9,12-14,39 and 42* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *5,8,9,12-14,39 and 42* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This Office Action is a reply to the Paper filed 28 February 2005 in response to the Non-Final Office Action mailed 27 September 2004. Claims 5-14, 39 and 42 and the nucleic acid encoding SEQ ID NO: 52 were considered in the 27 September Office Action. Claims 1-4, 6, 7, 10, 11, 15-38, 40, 41 and 43-49 were canceled and claims 5, 9 and 12 were amended in the 28 February Paper. Claims 5, 8, 9, 12-14, 39 and 42 are pending and under consideration to the extent that they read on a nucleic acid encoding the instant SEQ ID NO: 52.

Election/Restrictions

Claim 5, part (e) and claim 9, part (b), as amended, are directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: The claims have been amended to recite various single nucleotide polymorphisms which are disclosed in Table 11 (page 132-133) of the specification as SNP variants of the NOV1 nucleic acid (SEQ ID NO: 1). Absent evidence to the contrary, the SNPs are not within the scope of the elected nucleic acid encoding SEQ ID NO: 52.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claim 5, part (e) and claim 9, part (b) are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

Response to Amendment and Arguments

Rejection of claims 6, 7, 10 and 11 is rendered moot by the cancellation thereof.

Specification

Objection to the disclosure as containing informalities is **withdrawn** in view of the amendments to the specification.

Claim Rejections - 35 USC § 101

Claims 5, 8, 9, 12-14, 39 and 42 **stand rejected** under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well-established utility.

In response to the *prima facie* case of record, Applicant asserts that the application discloses a specific and substantial utility for the claimed invention as a marker to differentiate certain cancer tissues, such as certain breast cancers or certain ovarian cancers, from their corresponding normal tissues. Applicant cites data presented in Table 6 and Table 8 of the specification indicating that a nucleic acid molecule comprising SEQ ID NO: 1 is highly expressed in certain tissues, including certain breast and ovarian cancer tissues as compared to normal breast and ovarian tissues. Applicant also submits an alignment of the amino acid sequence encoded by SEQ ID NO: 1 with the sequence encoded by the claimed nucleic acid demonstrating similar but not identical sequence. Applicant concludes that these teachings support a specific and substantial utility of the claimed nucleic acids for differentiating certain cancer tissues from their corresponding normal tissues.

These arguments have been fully considered but are not deemed persuasive. First, even if one were to accept that the teachings cited by Applicant support a specific and substantial utility

for a nucleic acid comprising SEQ ID NO: 1 as a probe for differentiating cancer tissues from their corresponding normal tissues, reasonably confirming that the claimed nucleic acid (*i.e.*, the nucleic acid encoding SEQ ID NO: 52) can be used as a probe for differentiating cancer tissues from their corresponding normal tissues would require additional experimentation. The specification contains no data for expression of nucleic acids encoding SEQ ID NO: 52 and no disclosure of how the nucleic acid comprising SEQ ID NO: 1 is related to the claimed nucleic acid encoding SEQ ID NO: 52. For example, the nucleic acids might be related as duplicated genes, one might be a pseudogene or the genes might be related as allelic variants. However, as applicant admits on page 131 of the specification, even very closely related genes can exhibit distinct patterns of expression. At lines 20-24, the specification states, "[single nucleotide polymorphisms] occurring outside the region of a gene, or in an intron within a gene, do not result in changes in any amino acid sequence of a protein but may result in altered regulation of the expression pattern for example, alteration in temporal expression, physiological response regulation, cell type expression regulation, intensity of expression, stability of transcribed message." In view of this teaching, Applicant's contention that the claimed invention can be used for differentiating cancer tissues from their corresponding normal tissues is not supported by data obtained for SEQ ID NO: 1.

Furthermore, the data cited by applicant fail to reasonably establish that even the nucleic acid comprising SEQ ID NO: 1 can be used as a marker for cancer tissue. First, the Data presented in Table 6, which appears to have been obtained with various cancer cell lines, is not probative of utility as a cancer marker gene. It has been recognized for many years that cancer cell lines do not accurately represent cancer cells found in their natural state. For example,

Dermer (1994) *Bio/Technol.* 12:320 teaches, "[w]hen a normal or malignant body cell survives a crisis period and adapts to immortal life in culture, it takes an evolutionary-type step that enables the new line to thrive in its artificial environment. This step transforms a cell from one that is stable and differentiated to one that is not. Yet normal or malignant cells *in vivo* are not like that. This means that cell lines are really a new life form on Earth, neither human nor animal. Evidence of the contradictions between life on the bottom of a lab dish and in the body has been in the scientific literature for more than 30 years..." Thus, elevated expression *in vitro* might be a consequence of a variety of factors. Although the data presented in Table 8 does include comparison of expression in tumors with matched margin controls for two breast cancers and one ovarian cancer (page 122), these data are not sufficient to establish the utility of SEQ ID NO: 1 as a marker to distinguish certain breast and ovarian cancers from normal tissue. Pollack *et al.* (2002) *Semin. Oncol.* 9:280-285 teaches, "[i]n performing a microarray characterization of cancer, it often quickly becomes apparent that many genes, perhaps several dozen, behave in biologically or clinically interesting ways, meriting further evaluation as candidate diagnostic markers or therapeutic targets. A major challenge is to prioritize the many candidate genes for future investigations" (paragraph bridging the left and right columns on page 282) and, "[w]hile DNA microarray experiments characterize gene expression across many thousands of genes, typically only a small number (~10 to 50) of specimens are examined. Findings must be validated on a larger collection of clinical specimens" (first full paragraph in the right column on page 282). These teachings, particularly the teaching that a clinical sample size of 10-50 specimens is insufficient to validate utility as a diagnostic or therapeutic target, clearly illustrate that data such as those presented in the instant Tables 6 and 8 do not substantiate a diagnostic

utility for a claimed nucleic acid. The data, at best, support a possible utility which must be validated. Therefore, establishing that the claimed nucleic acid can be used as asserted in Applicant's arguments would clearly require additional experimentation and, therefore, the utility is not substantial.

Applicant's arguments have been fully considered but are not deemed persuasive in view of the record as a whole. Therefore, the claims stand rejected under 35 USC §101 as lacking a patentable utility.

Claim Rejections - 35 USC § 112, first paragraph, written description

Claims 5, 8, 9, 12-14, 39 and 42 **stand rejected** under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement.

In response to the *prima facie* case of record, Applicant submits that all the variants as defined in the amended claims are sufficiently described in the specification and can be used for the asserted utility.

This argument has been fully considered but is not deemed persuasive. It is presumed that the asserted utility referred to by Applicant is use as a probe for differentiating cancer tissues from their corresponding normal tissues as asserted in response to the rejection under 35 USC §101. However, given Applicant's admission that "[single nucleotide polymorphisms] occurring outside the region of a gene, or in an intron within a gene, do not result in changes in any amino acid sequence of a protein but may result in altered regulation of the expression pattern for example, alteration in temporal expression, physiological response regulation, cell type expression regulation, intensity of expression, stability of transcribed message" (*Id.*), the skilled

artisan would not have viewed the disclosure as demonstrating that Applicant was in position of the full scope of variants useful as a probe for differentiating cancer tissues from their corresponding normal tissues because the specification does not teach which nucleic acids within the scope of the claims have that utility. Therefore, the claims stand rejected under 35 USC §112, first paragraph, as lacking adequate descriptive support.

Claim Rejections - 35 USC § 112, first paragraph, enablement

Claims 5, 8, 9, 12-14, 39 and 42 **stand rejected** under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement.

In response to the *prima facie* case of record, Applicant cites the response to the rejection under 35 USC §101 and urges that the specification fully enables the skilled artisan to use the claimed nucleic acids for the asserted utility. This argument has been fully considered but is not deemed persuasive. Applicant is reminded that patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable. *See Brenner v. Manson,* 383 U.S. 519, 536, 148 USPQ 689, 696 (1966) (stating, in context of the utility requirement, that "a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion."). For the reasons set forth herein above, the specification fails to establish that even the nucleic acid comprising SEQ ID NO: 1, for which expression data are actually provided, can be used as Applicant now asserts, let alone the elected invention which is a nucleic acid encoding SEQ ID NO: 52. Given the unpredictability of the art, which is admitted in Applicant's specification (*Id.*) and evidenced by the teachings of Dermer *et al.* and Pollack *et al.*, establishing that any given nucleic acid within

the scope of the claims (*i.e.*, any nucleic acid encoding a mature form or variant of the polypeptide sequence set forth as SEQ ID NO: 52) could be used as a probe for differentiating cancer tissues from their corresponding normal tissues would require undue experimentation. Therefore, the claims are properly rejected under 35 USC §112, first paragraph, as lacking an enabling disclosure.

Claim Rejections - 35 USC § 112, second paragraph

Rejection of claims 5, 8, 9, 12-14, 39 and 42 under 35 U.S.C. 112, second paragraph, as being indefinite is **withdrawn** in view of the amendments to the claims.

Double Patenting

Provisional rejection of claims 5, 8, 9 and 12-14 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 20-28 of copending Application No. 10/287,971 is **withdrawn**. The claims of the '971 application have been amended such that they are now directed to subject matter that is patentably distinct from the subject matter claimed in the instant application.

Claim Rejections - 35 USC § 102

Claims 5, 9, 12-14, 39 and 42 **stand rejected** under 35 U.S.C. 102(a) as being anticipated by Shimkets *et al.* (12/28/2000) WO 00/78802.

In response to the *prima facie* case of record, Applicant asserts that the nucleic acid cited in the Office Action is not the work of "another" because the co-inventors Corine Vernet and

Ferenc Boldog of the instant application are also the inventors of the nucleic acid disclosed by Shimkets *et al.* Applicant states that an affidavit under Rule 1.131 will be submitted if the Examiner deems necessary.

Applicant is reminded, it is incumbent upon the inventors named in the application, to rebut a rejection under 35 U.S.C. 102(a) or (e), to provide a satisfactory showing by way of affidavit under 37 CFR 1.132 that the inventorship of the application is correct in that the reference discloses subject matter derived from the applicant rather than invented by the author, patentee, or applicant of the published application notwithstanding the authorship of the article or the inventorship of the patent or published application. In re Katz, 687 F.2d 450, 455, 215 USPQ 14, 18 (CCPA 1982). See MPEP 716.10. An assertion by Applicant's representative attributing the anticipatory subject matter to the instant inventors is insufficient to overcome a under 35 USC §102(a). Therefore, the claims stand rejected.

Claims 5, 12, 14, 39 and 42 **stand rejected** under 35 U.S.C. 102(b) as being anticipated by Webb *et al.* (1987) *DNA* 6:71-79 as evidenced by Sanger *et al.* (1977) *Proc. Natl. Acad. Sci. USA* 74: 5463-5467.

In response to the *prima facie* case of record, Applicant merely asserts that the claims as amended no longer encompass the nucleic acid disclosed in Webb *et al.* This argument has been fully considered but is not deemed persuasive. As described on page 7-8 of the previous Office Action, the claims are construed as follows:

The limitation "mature form", appearing in claim 5, is defined in the paragraph bridging pages 39-40 of the specification as "the product of a naturally occurring polypeptide or precursor

form or proprotein." Although the specification provides some examples of how a "mature form" of a polypeptide might be produced, these are explicitly identified as "nonlimiting". Therefore, the broadest reasonable interpretation of "mature form" according to the description provided encompasses a product of a naturally occurring polypeptide produced by any means. For example, the claim reads on a nucleic acid encoding any degradation product of the naturally occurring polypeptide.

The limitation "variant", appearing in claims 5, is understood based on the discussion in the first paragraph on page 38 as encompassing a protein "any of whose residues may be changed from the corresponding residue shown in Table 1B while still encoding a protein that maintains its endozepine-related protein precursor-like activities and physiological functions, or a functional fragment thereof. In the mutant or variant protein, up to about 60% percent [sic] of the residues may be so changed." Although claim 5 now recites that the substitutions are "conservative", conservative substitutions are defined in the section beginning on page 47 of the specification as encompassing any sequence that differs from the sequences explicitly set forth yet retaining "biological activity".

The amended claims still embrace nucleic acids encoding a mature form or variant of the polypeptide set forth as SEQ ID NO: 52. As stated in the previous Office Action, Webb *et al.* discloses a nucleic acid encoding a polypeptide that is 85% identical to the instant SEQ ID NO: 52 which polypeptide, absent evidence to the contrary, would retain "biological activity". Thus, the nucleic acid anticipates the nucleic acid encoding a mature form or variant of SEQ ID NO: 52 according to claim 5. Therefore, for reasons of record, claims 5, 12, 14, 39 and 42 are

anticipated by the teachings of Webb *et al.* as evidenced by Sanger *et al.* and stand rejected under 35 USC §102(b).

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Daniel M Sullivan whose telephone number is 571-272-0779. The examiner can normally be reached on Monday through Thursday 6:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel, Ph.D. can be reached on 571-272-0781. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Daniel M. Sullivan, Ph.D.

DAVID GUZO
PRIMARY EXAMINER